

## **REMARKS**

Review and reconsideration of the application in view of Applicants' amendments and following remarks are respectfully requested. Applicants herein cancel claims 29 and 47 without prejudice to or disclaimer of the subject matter therein. Applicants note claims 25 and 35-40 were previously canceled, and claims 41 and 42 were not entered. Claims 6-9, 18-20, 24, 32, and 48 are amended to correct typographical and grammatical errors, and to conform with amendments to the independent claims. Claim 3 has been amended to claim a Poisson distribution of microparticles, and is supported in the specification at least at page 5, lines 17-19, and page 12, lines 14-17. Independent claims 1, 27, 49, 50, and 51 are amended to more clearly point out the subject matter of the claimed invention, and are supported by the specification. In particular, the following features are supported in the specification as follows: that the gelling agent forms an immobilizing gel is supported at least at page 5, lines 25-26; that the gel includes a single layer of microspheres is supported at least at page 2, lines 27-30, and page 6, lines 10-12; that the microspheres are in random distribution is supported at least at page 5, lines 16-19, and Example 2 at page 12, lines 25-29; that the microspheres are evenly spread with a uniform density is supported in at least by Example 2 at page 11, lines 24-26; and that the microspheres are polymeric is supported throughout the application, and at least at page 5, line 26, and page 7, lines 1-11. Claim 44 is amended to include all the features of claim 27.

## **Interview**

Applicants thank Examiner Forman for the personal telephonic interview of April 28, 2004, between Examiner Forman, co-inventor Krishnan Chari, and Applicants' undersigned representative. During the interview, proposed claim amendments were presented and discussed, and each of the substantive rejections discussed with regard to the proposed claim amendments. Applicants' remarks regarding the substance of the interview are reflected in the above amendments and following remarks.

### **Rejoinder of Withdrawn Claims**

Claims 44-49 are withdrawn from consideration by the Patent Office as drawn to inventions distinct from the invention originally claimed. Applicants herein amend Claim 44 to include all the features of claim 27. Applicants note Claim 49 depends from claim 1, and includes all the features thereof. Rejoinder of claims 44 and 49, and the claims dependent therefrom, is appropriate and respectfully requested. Rejoinder is proper because process claims 44 and 49 include all the features of, or depend from, product claims already under consideration. No undue burden is placed on the Examiner by rejoinder because the subject matter of the claims is substantially the same as claims already searched. Applicants respectfully request rejoinder and consideration of claims 44-49.

### **Invention**

As discussed during the interview, Applicants invention as claimed is directed to either a coating composition for making a microarray, or a microarray, comprising (1) microspheres dispersed in a fluid, wherein the fluid contains a coating aid and a gelling agent, and wherein the gelling agent forms an immobilizing gel including a single layer of the microspheres, wherein the microspheres are in a random distribution such that the microspheres are evenly spread with a uniform density (claims 1, 27), or (2) polymeric microspheres dispersed in a fluid, the fluid comprising a coating aid and a gelling agent wherein the polymeric microspheres are-immobilized at random positions in a single layer upon sol-to-gel transition of the gelling agent to a gel (claims 50,51). Withdrawn claims 44 and 49 are directed to methods of making the microarrays. The single layer of immobilized microspheres in a random distribution is important in use of the microarray in high-throughput assays, wherein each microparticle must be individually identifiable at low magnification. Overlap or clustering of the microspheres would hinder identification of individual microspheres. Known processes for separating microspheres in a microassay are described, for example, in Walt et al., wherein the surface of a substrate is patterned chemically or physically to form specific attachment sites. In contrast, the claimed invention

achieves a single, random layer of microspheres by sol-to-gel transition of a gelling agent that is coated with the microspheres.

**35 U.S.C. §102(b) over Sutton et al.**

Claims 1-8, 13, 15-17, and 21 are rejected under 35 U.S.C. §102(b) as being anticipated by Sutton et al. (US 5,714,340). According to the Office Action, Sutton et al. discloses including a composition comprising microspheres dispersed in a fluid containing a coating aid and a gelling agent, wherein the gelling agent forms a gel capable of immobilizing the microspheres at random positions on a substrate. For at least the following reasons, Applicants respectfully traverse this rejection.

As discussed during the interview, Sutton et al. does not teach, disclose or suggest the subject matter of the claimed invention as set forth in independent claim 1, from which claims 2-8, 13, 15-17, and 21 depend. Sutton et al. is directed to an immunoassay element for assaying ligands, wherein the element includes a layer containing a labeled ligand, a bead spreading layer, a cross-linked hydrophilic polymer layer including receptors, and a support. Neither the beads of the bead spreading layer nor the receptors of the cross-linked hydrophilic polymer layer can be compared to the microspheres of the claimed invention as set forth in claim 1.

The beads of the bead spreading layer, as shown in Figure 1 of Sutton et al., form a stack, comprising multiple layers of beads. In contrast, the claimed invention has a single layer of microspheres.

The receptors, shown in Figures 3-5 of Sutton et al., and discussed at col. 10, lines 3-11, form clusters in the cross-linked hydrophilic polymer layer, as admitted by Examiner Forman during the interview. In contrast, the claimed invention is directed to microspheres that are immobilized in a random distribution such that the microspheres are evenly spread with a uniform density, as explained and exemplified in Example 2, at page 11, lines 21-28, of Applicants' specification. As admitted by Examiner Forman during the interview, the clustered receptors of Sutton are not "evenly spread" as claimed by Applicants. Further, as shown in Applicants' Example 2, without use of the claimed invention,

streaking can occur in the coating, wherein the streaking corresponds to aggregates of microspheres, such as those found in Sutton.

Sutton et al. does not teach all the elements of the claimed invention. For example, Sutton et al. does not teach at least a composition comprising microspheres in a single layer immobilized in a random distribution such that the microspheres are evenly spread with a uniform density, as agreed to by Examiner Forman during the interview. For at least the above reasons, reconsideration and withdrawal of the rejection are in order and are respectfully requested.

**35 U.S.C. §102(b) over Pierce et al.**

Claims 1-24, 26-34 and 43 are rejected under 35 U.S.C. §102(b) as being anticipated by Pierce et al. (US 4,258,001). According to the Office Action, Pierce et al. teaches a coating composition including microspheres dispersed in a fluid containing a coating aid and a gelling agent wherein the gelling agent forms a gel immobilizing the microspheres at random positions on a substrate. For at least the following reasons, Applicants traverse the rejection.

Pierce et al. does not teach, disclose or suggest the subject matter of the claimed invention as set forth in the cited claims, and as exemplified by independent claims 1 and 27. As discussed during the interview, Pierce et al. is directed to an element for analysis or transport of a liquid, wherein the element includes particles with an adhesive surface forming a three-dimensional structure. This is exemplified in Figures 2-14, cited in the Office Action as exemplary of the Pierce et al. teaching. As stated at col. 6, lines 49-51, of Pierce et al., formation of a coherent, three-dimensional lattice by organopolymeric particles is “an essential feature of the invention.” Applicants’ invention, as set forth in independent claims 1 and 27, and the claims dependent therefrom, has a single layer of microspheres immobilized in a random distribution. Pierce et al. does not teach, disclose, or suggest a single layer of microspheres, and in fact teaches away from two-dimensional structures. For at least the above reasons, reconsideration and withdrawal of the rejection are in order and are respectfully requested.

**§102(e) over Charych et al**

Claims 50 and 51 are rejected under 35 U.S.C. §102(e) as being anticipated by Charych et al (US 6,306,598). According to the Office Action, Charych et al. teaches a coating composition including microspheres dispersed in a fluid, wherein the fluid contains a precursor to a gelling agent capable of sol-to-gel transition, wherein the microspheres are randomly immobilized in the gel. For at least the following reasons, Applicants traverse the rejection.

Charych et al. does not teach, disclose or suggest the subject matter of the claimed invention as set forth in claims 50 and 51. As discussed in the interview with Examiner Forman, Charych et al. is directed to compositions useful for the detection of analytes, wherein the composition includes biopolymeric material immobilized on a support, wherein the biopolymeric material includes a plurality of polymerized self-assembling monomers and one or more nucleic acid ligands, as described at col. 2, l. 54-58. "Self-assembling monomers" are defined as molecules that spontaneously associate to form molecular assemblies that can themselves aggregate to form even larger assemblies. See col. 15, l. 44-53. Other embodiments described at col. 3, lines 45-51, include biopolymeric films, liposomes, tubules, braided assemblies, lamellar assemblies, helical assemblies, fiber-like assemblies, solvated rods, and solvated coils.

Claims 50 and 51 are directed to a coating composition or a microarray, respectively, wherein the coating includes polymeric microspheres randomly immobilized in a single layer in a gel formed by sol-to-gel transition of a fluid including the microspheres. The microspheres are polymeric, and do not constitute a self-organized molecular aggregate as defined by Charych et al. For at least the above reasons, as discussed in the interview, reconsideration and withdrawal of the rejection are in order and are respectfully requested.

**35 U.S.C. §103(a) over Walt et al. in view of McGall et al.**

Claims 1-11, 15-24, 27-29 and 31-34 are rejected under 35 U.S.C. §103(a) as being unpatentable over Walt et al. (WO 00/16101) in view of McGall et al. (US 6,147,205). According to the Office Action, Walt et al. discloses a coating composition comprising a gelling agent and microspheres dispersed in a

fluid, but does not disclose use of a coating aid. McGall et al. is cited for disclosure of a coating aid. Applicants traverse the rejection for at least the following reasons.

As admitted by Examiner Forman during the interview, the combination of Walt et al. and McGall et al. does not disclose or suggest the claimed invention. Walt et al. specifically discloses at p. 22, lines 10-16, a two-step process wherein the microspheres and a film-forming solution are applied separately. McGall et al. discloses compounds and methods for protecting chemical groups, and for forming compounds on an activated support. McGall et al. does not disclose or suggest gelation of a polymeric solution. McGall et al. discloses the use of polyvinyl alcohol and a coating agent, however, as shown by Applicants' Example 1 at page 9, lines 9-30, such a combination (formulation 2 - control) in and of itself does not form a gel. As admitted by Examiner Forman during the interview, Neither Walt et al. nor McGall et al., alone or in combination, discloses or suggests a fluid containing microspheres forming a gel immobilizing the microspheres, as set forth in Applicants' claims 1 and 27. For at least the above reasons, reconsideration and withdrawal of the rejection are in order.

**35 U.S.C. §103(a) over Anderson et al. in view of McGall et al.**

Claims 1-8, 12, 13, 24, and 27-34 were rejected under 35 U.S.C. §103(a) over Anderson et al. (U.S. Patent Publication No. 2002/0015952) in view of McGall et al. According to the Office Action, Anderson et al. discloses a coating composition comprising a gelling agent and microspheres wherein on gelling the microspheres become immobilized in the plane of coating and form a random pattern on the substrate. McGall et al. is cited as teaching a coating aid. For at least the following reasons, Applicants traverse the rejection.

As discussed with Examiner Forman, and as described at page 2, paragraph 0012, Anderson et al. is directed to forming a coating of biological agents in discrete tubes or fibers. The tubes or fibers are then cross-sectioned, and the cross-sections applied to a substrate. Paragraphs 0131-0133 of Anderson et al., cited in the Office Action, clearly describe the formation and attachment of such cross-sections to a substrate, which substrate can be flexible or solid. As

agreed to by Examiner Forman during the interview, because the biological agents are applied to the substrate of Anderson within cross-sections of tubes or fibers, the substrate of Anderson does not achieve a random distribution of microspheres such that the microspheres are evenly spread with a uniform density, as claimed by Applicants. Further, as known to one skilled in the art, cross-sectioning of a filled tube or fiber is not a precise art, and it is unlikely a single layer of biological agents could be achieved by the methods of Anderson et al., in contrast to the claimed invention. *See*, for example, paragraphs 132 and 141-142 of Anderson et al., discussing the thickness of tube sections to be applied to a substrate, and the three-dimensional structures formed by multiple layers of molecules bound to the substrate.

McGall et al. is cited for disclosure of a coating aid, and does not overcome the above-stated deficiencies of Anderson et al., as admitted by Examiner Forman. Anderson et al. and McGall et al., alone or in combination, do not disclose or suggest at least microspheres immobilized in a single layer on a substrate upon gelation of a gelling agent as required by independent Claims 1 and 27 of the subject application. For at least the above reasons, reconsideration and withdrawal of the rejection are in order.

**35 U.S.C. §103(a) over Walt et al. in view of McGall et al. and Anderson et al.**

Claims 12-14 and 30 were rejected under 35 U.S.C. §103(a) over Walt et al. in view of McGall et al. as applied to Claims 1 and 27 above, and further in view of Anderson et al. Applicants traverse the rejection because, as discussed above, none of the references, alone or in combination, discloses or suggests a single layer of microspheres immobilized on a substrate upon gelation of a gelling agent, as agreed to by Examiner Forman during the interview. For at least the above reasons, reconsideration and withdrawal of the rejection are in order.

**35 U.S.C. §103(a) over Walt et al. in view of McGall et al. and Chang et al.**

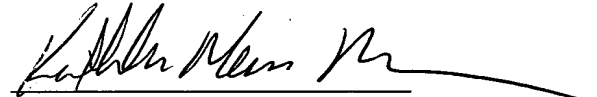
Claim 26 was rejected under 35 U.S.C. §103(a) over Walt et al. in view of McGall et al. as applied to Claims 1 and 27 above, and further in view of Chang et al. (U.S. Patent No. 4,873,102). For at least the following reasons, Applicants traverse the rejection.

Walt et al. in view of McGall et al. is discussed above. Chang et al. is cited in the Office Action for a teaching of emulsion polymerization. However, Chang et al. does not overcome the deficiencies of Walt et al. or McGall et al. Specifically, none of the references, alone or in combination, discloses or suggests microspheres immobilized on a substrate upon gelation of a gelling agent, as agreed to by Examiner Forman during the interview. For at least the above reasons, reconsideration and withdrawal of the rejection are in order.

All of claims 1-14, 26-28, 30-34, 43-46, and 48-51 are believed to be patentable over the cited references for at least the reasons stated herein. Further action in the form of a Notice of Allowance is thus respectfully solicited.

Should the Examiner require anything further, or have any questions, the Examiner is invited to contact Applicants' undersigned representative.

Respectfully submitted,

A handwritten signature in dark ink, appearing to read 'Kathleen Neuner Manne', is written over a horizontal line.

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